

[0026] In another preferred embodiment, the magnetic microchannel comprises a gradient-inducing feature. In this embodiment, one or more structural features are provided within the channel that enhance or induce a magnetic field gradient within magnetic microchannel. For example, in one embodiment a series of sawtooth ridges are provided, coated with a magnetic material. Gradient-inducing features are further described below.

[0027] In addition to the magnetic microchannels, there can also be other components integral to the microfluidic device. These include labeling chambers for attaching a magnetic label to a component in the sample; releasing chambers for releasing a magnetic label from the labeled component, cell handling modules for cell concentration, cell lysis, and cell removal; separation modules for separation of the desired target analyte from other sample components; and reaction modules for chemical or enzymatic reactions on the target analyte. The devices of the invention can also include one or more wells for sample manipulation, waste or reagents; microchannels to and between these wells; valves to control fluid movement; on-chip pumps; and detection modules for the detection of target analytes, as is more fully described below. The devices of the invention can be configured to manipulate one or multiple samples or analytes.

[0028] In an experiment, the biological sample is labeled with magnetic labels either in a separate device or within a labeling chamber integral to the microfluidic device. The labeled sample is then subjected to processing in a magnetic microchannel. Depending on the magnetic microchannels that are used, a magnetic field is generated within the channel either by an external magnet or by magnetizing magnetic materials within the channel. Materials that are labeled by magnetic labels will generally be retained in the magnetic microchannel, and those that are not captured in the channel can be collected for further processing or disposed as wastes. When target analytes are retained, they may be washed while captured within the microchannel. After the optional washing step, the target analytes can be directly detected within the magnetic microchannel, further processed in the microchannel, or eluted from the microchannel for further processing and/or detection. If processed inside the channel, the end product of the processing can also be eluted for further treatment and/or detection.

[0029] Accordingly, the present invention provides devices and methods for the detection of target analytes in biological samples. By "biological sample" herein is meant a sample containing at least one biological material. The list of biological materials includes but is not limited to microorganisms such as protozoa, bacteria, yeast, and other fungi, viruses, cultured cells or cells prepared from multi-cellular organisms including mammals and other vertebrates; bodily fluids including blood, lymph, saliva, vaginal and anal secretions, urine, feces, perspiration and tears; solid tissues, including liver, spleen, bone marrow, lung, muscle, brain, etc. Also appropriate are organelles or suborganelles of eucaryotic cells, and aggregates or individual molecules including proteins, glycoproteins, lipoproteins, carbohydrates, lipids, nucleic acids, and the like.

[0030] By "target analyte" or "analyte" or grammatical equivalents herein is meant any molecule, compound or particle to be detected. As outlined below, target analytes

preferably bind to binding ligands, as is more fully described above. As will be appreciated by those in the art, a large number of analytes may be detected using the present methods; basically, any target analyte for which a binding ligand described herein, may be made may be detected using the methods of the invention.

[0031] Suitable analytes include organic and inorganic molecules, including biomolecules. In a preferred embodiment, the analyte may be an environmental pollutant (including pesticides, insecticides, toxins, etc.); a chemical (including solvents, polymers, organic materials, etc.); therapeutic molecules (including therapeutic and abused drugs, antibiotics, etc.); biomolecules (including hormones, cytokines, proteins, lipids, carbohydrates, cellular membrane antigens and receptors (neural, hormonal, nutrient, and cell surface receptors) or their ligands, etc); whole cells (including procaryotic (such as pathogenic bacteria) and eukaryotic cells, including mammalian tumor cells); viruses (including retroviruses, herpesviruses, adenoviruses, lentiviruses, etc.); and spores; etc. Particularly preferred analytes are environmental pollutants; nucleic acids; proteins (including enzymes, antibodies, antigens, growth factors, cytokines, etc); therapeutic and abused drugs; cells; and viruses.

[0032] In a preferred embodiment, the target analyte is a nucleic acid. By "nucleic acid" or "oligonucleotide" or grammatical equivalents herein means at least two nucleotides covalently linked together. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, as outlined below, nucleic acid analogs are included that may have alternate backbones, comprising, for example, phosphoramidate (Beaucage et al., *Tetrahedron* 49(10):1925 (1993) and references therein; Letsinger, J. *Org. Chem.* 35:3800 (1970); Sprinzl et al., *Eur. J. Biochem.* 81:579 (1977); Letsinger et al., *Nucl. Acids Res.* 14:3487 (1986); Sawai et al., *Chem. Lett.* 805 (1984); Letsinger et al., *J. Am. Chem. Soc.* 110:4470 (1988); and Pauwels et al., *Chemica Scripta* 26:141 91986)), phosphorothioate (Mag et al., *Nucleic Acids Res.* 19:1437 (1991); and U.S. Pat. No. 5,644,048), phosphorodithioate (Briu et al., *J. Am. Chem. Soc.* 111:2321 (1989), O-methylphosphoramidite linkages (see Eckstein, *Oligonucleotides and Analogues: A Practical Approach*, Oxford University Press), and peptide nucleic acid backbones and linkages (see Egholm, *J. Am. Chem. Soc.* 114:1895 (1992); Meier et al., *Chem. Int. Ed. Engl.* 31:1008 (1992); Nielsen, *Nature*, 365:566 (1993); Carlsson et al., *Nature* 380:207 (1996), all of which are incorporated by reference). Other analog nucleic acids include those with positive backbones (Denpey et al., *Proc. Natl. Acad. Sci. USA* 92:6097 (1995); non-ionic backbones (U.S. Pat. Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowski et al., *Angew. Chem. Intl. Ed. English* 30:423 (1991); Letsinger et al., *J. Am. Chem. Soc.* 110:4470 (1988); Letsinger et al., *Nucleoside & Nucleotide* 13:1597 (1994); Chapters 2 and 3, *ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research"*, Ed. Y. S. Sanghui and P. Dan Cook; Mesmaeker et al., *Bioorganic & Medicinal Chem. Lett.* 4:395 (1994); Jeffs et al., *J. Biomolecular NMR* 34:17 (1994); *Tetrahedron Lett.* 37:743 (1996)) and non-ribose backbones, including those described in U.S. Pat. Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, *ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research"*, Ed. Y. S. Sanghui and P. Dan Cook.